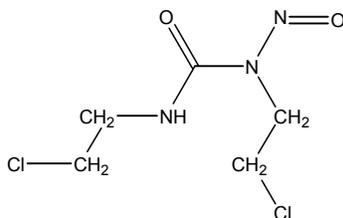


BIS(CHLOROETHYL) NITROSOUREA

CAS No. 154-93-8

First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

bis(Chloroethyl) nitrosourea (BCNU) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1981, 1982, 1987). When administered intraperitoneally or intravenously, bis(chloroethyl) nitrosourea induced lung tumors including adenocarcinomas and neurogenic tumors in rats. When administered by intraperitoneal injection, the compound induced malignant tumors in the peritoneal cavity. Other studies of bis(chloroethyl) nitrosourea in rats and mice were determined to provide insufficient data for evaluation by an IARC Working Group (IARC 1981, 1982, 1987).

There is limited evidence for the carcinogenicity of bis(chloroethyl) nitrosourea in humans (IARC 1981, 1982, 1987). No epidemiological studies on the effect of bis(chloroethyl) nitrosourea in humans were available, but bis(chloroethyl) nitrosourea is associated with acute nonlymphocytic leukemia following its use with other anticancer therapies in the treatment of previously existing cancer (IARC 1987).

PROPERTIES

bis(Chloroethyl) nitrosourea is an orange-yellow solid that is slightly soluble in water, soluble in ethanol, and highly soluble in lipids. This compound is sensitive to oxidation and hydrolysis, subsequently forming alkylating and carbamoylating intermediates. When heated to decomposition, it emits toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NTP 2001).

USE

bis(Chloroethyl) nitrosourea has been used since 1971 as an antineoplastic agent in the treatment of Hodgkin's lymphoma, multiple myeloma, and primary or metastatic brain tumors. It has also been reported to have antiviral, antibacterial, and antifungal activity, but no evidence was found that it is currently used for these purposes (IARC 1981). bis(Chloroethyl) nitrosourea is also used to treat melanoma and renal cell tumors (NTP 2001).

PRODUCTION

The USITC does not list any production volume for bis(chloroethyl) nitrosourea (USITC 1995). Chem Sources (2001) identified three U.S. suppliers of the compound. In 1981, bis(chloroethyl) nitrosourea was believed to be produced by only one U.S. company in an undisclosed quantity and was available in the U.S. in vials containing 100 mg (IARC 1981).

EXPOSURE

The primary routes of potential human exposure to bis(chloroethyl) nitrosourea are injection, inhalation, and dermal contact. It was administered to patients in doses of 100 to 250 mg/m² body surface by intravenous injection daily, for 2 or 3 days (IARC 1981). The National Occupational Exposure Survey (1981-1983) estimated that 5,596 total workers, including 2,809 women, potentially were exposed to bis(chloroethyl) nitrosourea in the work place (NIOSH 1984). Health professionals such as pharmacists, nurses, and physicians who handle this drug may potentially be exposed during drug preparation, administration, or cleanup; however, the risks can be avoided through use of containment equipment and proper work practices (Zimmerman *et al.* 1981). Potential occupational exposure to bis(chloroethyl) nitrosourea may also occur for workers involved in the formulation and packaging of the pharmaceuticals (IARC 1981).

REGULATIONS

Bis(chloroethyl) nitrosourea is used as a pharmaceutical and in low quantities relative to other chemicals; therefore, it is of little regulatory concern to EPA. However, there may be a small pollution problem relative to hospital wastes.

FDA regulates bis(chloroethyl) nitrosourea under the Food, Drug, and Cosmetic Act (FD&CA) as a prescription drug, approved for human use. FDA requires warning labels on bis(chloroethyl) nitrosourea regarding its potential carcinogenicity, mutagenicity, teratogenicity, and/or fertility impairment.

OSHA regulates bis(chloroethyl) nitrosourea under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 37.

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bis(Chloroethyl) nitrosourea (Continued)

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